REMARKS

Claims 1-2, 5-19, 21-29, 31-32, 34-44, 46 and 48-57 are pending in this application. The following rejections have been maintained in the final Office Action:

(1) claims 1-2, 5-19, 21-29, 31, 32, 34-44, 46, 48-57, provisionally, under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 1-39 of copending U.S. Application No. 09/334,130;

(2) claims 1-2, 5-19, 21-29, 31, 32, 34-44, 46, 48-57 as failing to meet the written description requirement under 35 U.S.C. § 112, first paragraph;

(3) claims 1-2, 5-19, 21-29, 31, 32, 34-44, 46, 48-57 as not being enabling under 35 U.S.C. § 112, first paragraph; and

(4) claims 1-2, 7-11, 14-19, 21, 26-28, 34, 39-42, and 55-56 as anticipated by US-A-5,607,691 under 35 U.S.C. § 102(b).

All other rejections of the claims have been withdrawn.

The Examiner has requested a copy of the MPEP section to which applicant refers in his response of December 27, 2001. Applicant, however, did not refer to the MPEP in that response but, rather, Rule 98(d) (*i.e.*, 37 C.F.R. 1.98(d)), to which the Examiner is believed to have access.

Amendment to Claims

Applicants are herein cancelling claims 21-25, 34-38, 44 and 48-52, without prejudice, and amending claims 5, 29, 39, 43, 53 and 55-57. More specifically, applicant is amending claims 5 and 29 to present them as independent claims; amending claims 39, 43 and 53 to incorporate specific arylpropionic acids; and amending 55-57 to correct claim dependency and antecedent bases for each of the claims. Upon entry of the amendment, claims 1-2, 5-19, 26-29, 31-32, 39-43, 46 and 53-57 will be pending.

Applicants submit that the amendment to the claims does not introduce new matter and is fully supported by the specification and claims, as originally filed. Applicants request the Examiner to enter the amendment under 37 C.F.R. § 1.116(b) because the amendments to

the claims either cancel claims, comply with requirements of form expressly set forth in a previous Office Action, or present the rejected claims in better form for consideration on appeal.

Provisional Obviousness-type Double Patenting Rejection

Claims 1-2, 5-19, 26-29, 32, 39-44, 46, 53, 55-57 are provisionally rejected underthe judicially-created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-39 of co-pending U.S. Application No. 09/334,130. Applicant requests that the this rejection be deferred pending some identification of allowable subject matter, as it likely can be readily resolved (depending upon the subject matter allowed) through the filing of a suitable terminal disclaimer.

Lack of Written Description Rejection

The rejection has been maintained of claims 1, 2, 5-19, 21-29, 31, 32, 34-44, 46, 48-57 under 35 U.S.C. § 112, first paragraph, for allegedly failing to meet the written description requirement because the Examiner is of the view that the number of combinations arylpropionic acids and proteins that applicant explicitly identifies in the specification allegedly is not "adequate" for those skilled in the art to recognize that applicant was in possession of the claimed subject matter (Office Action at page 3). Inherent in this allegation is the presumption that there exists a certain number of combinations that, if disclosed, would have been "adequate." The Office Action, however, does not identify the number of combinations that allegedly would have been necessary to comply with the written description requirement of § 112. Applicant respectfully requests that this number officially be made of record, along with the Examiner's rationale in setting it. This information appears to have been the key factor influencing the Examiner's rejection of the claims, and accordingly must be made of record so that Applicant and the Board can assess whether or not it actually provides a valid basis for rejection. Applicant also requests that the Examiner provide all of the evidence of which he is aware supporting the allegation that "[o]ne in the art would not recognize the disclosure of the limited number of species is representative of

the genus claimed" (Office Action at page 4). At present, the statement is unsupported, and thus constitutes the Examiner subjective opinion.

Lack of Enablement Rejection

The rejection has been maintained of claims 1-2, 5-19, 21-29, 31, 32, 34-44, 46, 48-57 under 35 U.S.C. § 112, first paragraph, because the specification allegedly would not enable those skilled in the art to practice the claimed inventions. The Examiner, however, still has not identified any evidence suggesting that those skilled in the art would be unable to practice the claimed inventions. The Examiner alleges that the teaching of the Kleinberg reference is relevant, but is not seen why the reference's teaching suggests any lack of enablement. The reference, for example, teaches that one seeking to change the activity of a receptor needs to use a molecule that binds the receptor in a precise manner. The claims, however, do not require that there be this type of change in receptor activity and, as a result, do not require such precise binding. Rather, the claims are more generally directed to compounds that interact with proteins. Accordingly, the teaching of the Kleinberg reference is not relevant to enablement of applicant's claims. The McLure is similarly irrelevant, because it clearly does not support the Examiner's allegation that arylpropionic acids would be expected to bind one protein but not another. As noted in the Office Action dated October 3, 2001, the McLure reference does not compare the relative binding of arylpropionic acids to different proteins, but the relative binding of an arylpropionic acid to a protein and a "membrane preparation." Moreover, the reference does not teach that the arylpropionic acid fails to bind the membrane preparation but, rather, that it binds in a nonspecific manner (McClure reference at page 455). Applicant submits that he has adequately described how to make and use the claimed arylpropionic acid-oligonucleotide conjugates, and that any experimentation that might be needed to carry out the claimed invention with a protein other than albumin would not be unduly burdensome to one of ordinary skill in art armed with the disclosure. *In re Angstadt*, 537 F.2d 498, 190 USPQ 214 (C.C.P.A. 1976).

Accordingly, applicant respectfully requests the Examiner to withdraw the rejection of claims 1-2, 6-19, 26-28, 31-32, 39-43, 46 and 53-57, as amended, under 35 U.S.C. § 112 (first paragraph) as not adequately enabled.

Novelty Rejection

The rejection has been maintained of claims 1-2, 7-11, 14-19, 21, 26-28, 34, 39, 40, 41, 42, 55, and 56 as allegedly being anticipated by US-A-5,607,691 ("the Hale patent"). Applicant traverses this rejection the Hale patent does not "clearly and unequivocally" disclose any claimed invention.

To anticipate, a reference must "clearly and unequivocally disclose the claimed [invention] or direct those skilled in the art to the [invention] without any need for picking, choosing and combining various disclosures not directly related to each other by the teachings of the cited reference." *Akzo v. U.S.I.T.C.*, 808 F.2d 1471, 1480 (Fed. Cir. 1986) (citing *In re Arkley*, 455 F.2d 586, 587 (C.C.P.A. 1972)); *In re Schaumann*, 572 F.2d 312, 314 (C.C.P.A. 1978) ("By having to select [a variable] from among the many possibilities which R in the structural formula [of the reference] may be, . . . does not give rise to the claimed compound being fully anticipated by the reference."). The Hale patent does not anticipate the instant claims because one of ordinary skill in the art would, by the Examiner's own admission, have to engage in substantial "picking, choosing and combination" from among the patent's disclosure to produce any claimed invention. For example, the Hale patent discloses over 40 compounds suitable as "effector groups" only one of which is an arylpropionic acid with hundreds of possible pharmaceutical agents. One of ordinary skill in the art would have had, at most, very long odds of selecting, a compound that fell within the scope of the present claims. Given the breadth of disclosure provided by the Halepatent, the reference cannot be said to "clearly and unequivocally disclose[s] the claimed invention." *Akzo*, 808 F.2d at 1480. Accordingly, applicant respectfully requests reconsideration and withdrawal of the rejection under § 102.

Conclusions

Applicant requests the Examiner to:

(1) enter the amendment to the claims;

(2) reconsider and withdraw the rejections of the claims; and

(3) pass claims 1-2, 5-19, 26-29, 31-32, 39-43, 46 and 53-57to allowance.

If the Examiner is of a contrary view, the Examiner is requested to contact the undersigned attorney at (215) 557-3861.

Attached hereto is a marked-up version of the changes made to the specification and the claims by the current amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Respectfully submitted,

Wendy A. Choi

Wendy A. Choi
Registration No. 36,697

Date: *September 30, 2002*

WOODCOCK WASHBURN LLP
One Liberty Place - 46th Floor
Philadelphia, PA 19103
Telephone : (215) 568-3100
Facsimile : (215) 568-3439

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

Please cancel claims 21-25, 34-38, 44 and 48-52, without prejudice, and rewrite claims 5, 29, 39, 43, 53 and 55-57 to read as follows:

1. (amended) An oligomeric compound conjugated to an arylpropionic acid that interacts with a protein.

2. The oligomeric compound of claim 1 wherein said arylpropionic acid binds to said protein.

5. (twice amended) An oligomeric compound conjugated to an arylpropionic acid, [The oligomeric compound of claim 1] wherein said arylpropionic acid is ibuprofen, suprofen, fenbufen, ketoprofen, (S)-(+)-pranoprofen, or carprofen.

6. (amended) The oligomeric compound of claim 5 wherein said arylpropionic acid is ibuprofen.

7. The oligomeric compound of claim 1 wherein said protein is a cellular, serum or vascular protein.

8. The oligomeric compound of claim 7 wherein said protein is a serum protein.

9. The oligomeric compound of claim 8 having a K_d lower than 20 μM with at least one serum protein.

10. The oligomeric compound of claim 8 wherein said serum protein is albumin, an immunoglobulin, α-2-macroglobulin, α-1-glycoprotein or a lipoprotein.

11. (amended) The oligomeric compound of claim 1 further including a linking group attaching said arylpropionic acid to said oligomeric compound.

12. The oligomeric compound of claim 11 wherein said linking group is 6-aminohexyloxy.

13. (amended) The oligomeric compound of claim 1 wherein said compound comprises a plurality of nucleosides connected by covalent internucleoside linkages.

14. The oligomeric compound of claim 13 wherein said linkages are phosphodiester linkages.

15. The oligomeric compound of claim 13 wherein said linkages are phosphorothioate linkages.

16. The oligomeric compound of claim 13 wherein said linkages are non-phosphorus containing linkages.

17. The oligomeric compound of claim 13 wherein at least one of said nucleosides bears a 2'-substituent group.

18. The oligomeric compound of claim 17 wherein said 2'-substituent group is O-alkylalkoxy.

19. The oligomeric compound of claim 18 wherein said 2'-substituent group is methoxyethoxy.

21. CANCELLED

22. CANCELLED

23. CANCELLED

24. CANCELLED

25. CANCELLED

26. (amended) A method of increasing the concentration of an oligonucleotide in serum comprising the steps of:

(a) selecting an arylpropionic acid that is known to bind to a serum protein;

(b) conjugating said arylpropionic acid to said oligonucleotide to form a conjugated oligonucleotide; and

(c) adding said conjugated oligonucleotide to said serum.

27. The method of claim 26 wherein said serum protein is albumin, an immunoglobulin, α-2-macroglobulin, α-1-glycoprotein or a lipoprotein.

28. The method of claim 26 wherein said serum protein is albumin.

29. (amended) [The method of claim 26] A method of increasing the concentration of an oligonucleotide in serum comprising the steps of:

conjugating [wherein said arylpropionic acid is] ibuprofen, suprofen, fenbufen, ketoprofen, (*S*)-(+)-pranoprofen or carprofen to said oligonucleotide to form a conjugated oligonucleotide; and

adding said conjugated oligonucleotide to said serum.

31. (amended) The method of claim 26 wherein said arylpropionic acid is ibuprofen.

32. The method of claim 31 wherein said protein is albumin.

34. CANCELLED

35. CANCELLED

36. CANCELLED

37. CANCELLED

38. CANCELLED

39. (twice amended) A method of increasing the capacity of serum for an oligonucleotide comprising the steps of:

(a) selecting an arylpropionic acid that is known to bind to a serum protein, wherein said arylpropionic acid is ibuprofen, suprofen, fenbufen, ketoprofen, (*S*)-(+)-pranoprofen or carprofen ;

(b) conjugating said arylpropionic acid to said oligonucleotide to form a conjugated oligonucleotide; and

(c) adding said conjugated oligonucleotide to said serum.

40. (amended) The method of claim 39 wherein said serum protein is a protein having a binding site for said arylpropionic acid.

41. The method of claim 39 wherein said serum protein is a protein having a binding site for said oligonucleotide.

42. (amended) The method of claim 39 wherein said serum protein is a protein having a binding site for said oligonucleotide and a binding site for said arylpropionic acid; wherein said binding site for said oligonucleotide is distinct from said binding site for said arylpropionic acid.

43. (twice amended) A method of increasing the binding of an oligonucleotide to a portion of the vascular system comprising the steps of:

(a) selecting an arylpropionic acid that is known to bind to a protein that resides, in part, in the circulating serum and in part in a non-circulating portion of the vascular system

wherein said arylpropionic acid is ibuprofen, suprofen, fenbufen, ketoprofen, (*S*)-(+)-pranoprofen, or carprofen;

(b) conjugating said arylpropionic acid to said oligonucleotide to form a conjugated oligonucleotide; and

(c) adding said conjugated oligonucleotide to said vascular system.

44. CANCELLED

46. (amended) The method claim 43 wherein said arylpropionic acid is ibuprofen.

48. CANCELLED

49. CANCELLED

50. CANCELLED

51. CANCELLED

52. CANCELLED

53. (twice amended) A method of promoting cellular uptake of an oligonucleotide in a cell comprising the steps of:

(a) selecting a protein that resides on the cellular membrane and extends, at least in part, on the external side of said membrane;

(b) selecting an arylpropionic acid that is known to bind to said protein

wherein said arylpropionic acid is ibuprofen, suprofen, fenbufen, ketoprofen, (*S*)-(+)-pranoprofen, or carprofen;

(c) conjugating said arylpropionic acid to said oligonucleotide to form a conjugated oligonucleotide; and

(d) exposing said cell to said conjugated oligonucleotide.

54. (amended) The method of claim 53 wherein said protein is a cell surface integrin.

55. (amended) The [oligonucleotide] oligomeric compound of claim 10 wherein said serum protein is human serum albumin.

56. (amended) The [oligonucleotide] method of claim 28 wherein said serum protein is human serum albumin.

57. (amended) The [oligonucleotide] method of claim 32 wherein said serum protein is human serum albumin.